

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/003512

International filing date (day/month/year)
16.08.2004

Priority date (day/month/year)
15.08.2003

International Patent Classification (IPC) or both national classification and IPC
G01N33/68

Applicant
UNIVERSITE DE GENEVA

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/003512

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☒ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 28-32 (in full); 1-26, 32-34 (in part)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 28-32 (in full); 1-26, 32-34 (in part)
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/003512

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 27 (in full), 1-26 and 32-34 (in part)

Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, Inventive step or Industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|-------------|
| Novelty (N) | Yes: Claims | 1-27, 32-34 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-27, 32-34 |
| Industrial applicability (IA) | Yes: Claims | 1-27, 32-34 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

5. Claims 31 (in full); 1-26 and 32-34 (in part): Apo AI as diagnostic marker for stroke

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The only subject matter common to all inventions is the provision of markers for diagnosis of stroke in general and for distinguishing between haemorrhagic and ischemic forms of stroke in particular.

D1 however discloses, that Antithrombin III is significantly decreased in cardioembolic and thrombotic stroke, both ischemic forms of stroke, but not different from the control group in lacunar stroke (a haemorrhagic form of stroke), rendering the single, general concept not novel.

Thus such subject matter can not form the basis for a single general inventive concept according to Rule 13.1 PCT.

Therefore the present application lacks unity as required by Art. 17(3)(a) and Rule 13 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Art. 33(3) PCT

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of **claims 1-27 and 32-34** does not involve an inventive step in the sense of Article 33(3) PCT.

Documents D1 and D2, both relevant prior art to the subject-matter of **claims 1, 13, 23 and 32**, disclose, that apolipoprotein CIII (ApoC III) is a risk factor for atherosclerosis and ischemic stroke. Vaccination against ApoCIII on the other hand protects from atherosclerosis and related diseases like ischemic stroke. Document D3 moreover discloses, that certain polymorphisms in the Apo CIII gene predispose for atherosclerosis and related diseases, like ischemic stroke.

The subject-matter of claims 1, 13, 23 and 32 differs therefrom in that, ApoCIII is claimed to be a diagnostic marker for ischemic stroke.

The problem to be solved by the present invention may therefore be regarded as

providing markers for the diagnosis of ischemic stroke.

The solution proposed in claims 1, 13, 23 and 32 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons. If a certain marker is considered prognostic for a certain disease and causally involved in the development of the disease, it will be also increased, when the disease becomes acute. Therefore, the use of ApoCIII as a diagnostic marker for ischemic stroke is considered obvious.

Dependent **claims 2-12, 13-22, 23-26 and 33-34** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, see document D4 and the corresponding passages cited in the search report.

2. Art. 33(4) PCT

Claims 1-27 and 32-34 are industrially applicable.